REMARKS/ARGUMENTS

Claims Status

Claims 1-7, 9-21, 24 and 26 are pending. Claims 1-3, 5, 6, 11, 13, 14 and 21 are currently amended for grammatical purposes and to improve readability. Claim 1 is also amended to clarify (1) that "HPLC/fluorescence detection" (see claim 3) refers to "a combination of HPLC and fluorescence detection", and (2) that the fluorescent and/or peptide fractions are applied to "mass spectrometry or MS/MS analysis" (see claim 2). Claim 21 is also amended to correct typographical errors as noted by the Office. Claims 8, 22 and 23 are canceled without prejudice. Claim 26 is added and finds support in original claim 1. Claim 26 differs from claim 1 in that claim 1 includes alternative "applying" steps after the separation of the fluorescent derivative, whereas claim 26 positively recites only one of the two alternatives. No new matter is believed to have been entered.

Specification Objection

The specification has been objected to for not including a section listing figures 1-12 (e.g., a Brief Description of the Drawings). Applicants point out that pages 60-61 include such a section. Accordingly, Applicants request withdrawal of this objection.

Claim Objections

A. Claims 21 and 22 are objected to for typographical errors. As stated above, claim 21 has been amended to correct these errors and claim 22 is canceled. Accordingly, Applicants request withdrawal of these objections.

B. Claim 22 has been objected to for failing to further limit the claim from which it depends. As claim 22 has been canceled, this objection is moot. Accordingly, Applicants request withdrawal of this objection.

§112, 2nd paragraph, Rejections

Claims 1-14 and 23 (namely claims 1-3, 5, 6, 8 and 23) have been rejected as indefinite for numerous reasons discussed in the outstanding Office Action. As explained above, claims 1-3, 5 and 6 have been amended for grammatical purposes and to improve readability. In addition, these claims have been amended for continuity of antecedent basis. Furthermore, claims 8 and 23 have been canceled. Accordingly, Applicants submit that the abundant amendments to the claims obviate the numerous indefinite rejections. As such, Applicants request withdrawal of these rejections.

§102(e) and §103(a) Rejections

Claims 1-9 and 15 are rejected as anticipated by Patricelli (US 7,179,655). Claim 10 is rejected as obvious in view of the combination of Patricelli and Goodlett (US 6,629,040). Claims 11 and 12 are rejected as obvious in view of the combination of Patricelli and Andersson (US 6,653,625). Claims 13 and 14 are rejected as obvious in view of the combination of Patricelli and Toyo'oka (Anal. Chem. 1984, 56, 2461-2464). Claims 16-18, 20 and 23 are rejected as obvious in view of Patricelli. Claim 19 is rejected as obvious in view of the combination of Patricelli and Srinivasan (US 2007/0065343). Applicants respectfully traverse this rejection.

A. Background of the Present Invention

An important objective in the post-genome area is the detection of trace amounts of expressed protein/peptide expressed through genes, and the separation and identification thereof.

In the past, peptide fingerprinting following two-dimensional electrophoresis was commonly used to achieve this objective. However, this method had problems with

reproducibility of the method due to the complex procedure. Separation and identification methods using multi-dimensional high-performance liquid chromatography (multi-dimensional HPLC), and techniques using ICAT have recently been proposed to overcome this problem.

Among these methods, methods for separating and identifying protein/peptide directly by multi-dimensional HPLC have the shortcoming of requiring considerable labor and time since all proteins/peptides are processed simultaneously.

In addition, methods using ICAT attempt to comprehensively analyze protein/peptide by labeling the thiol groups of thiol-containing protein/peptide with an isotope-coded affinity tag (ICAT) reagent, capturing the protein/peptide with a biotin-coupled column, subjecting all of the proteins/peptides to enzymatic hydrolysis, separating the resulting mixture of peptide fragments by HPLC, and carrying out mass spectrometry on the peptide fragments with a mass spectrometer (MS).

However, since this method involves subjecting all thiol-containing protein/peptide to enzymatic hydrolysis, it has the shortcoming of fragments of non-target protein/peptide present in large amounts impairing detection and identification of target trace protein/peptide, thereby creating the need to achieve further improvement in this technical field.

With the foregoing in view, as a result of conducting extensive research for the purpose of radically solving the above-mentioned problems of the prior art, the inventors of the present invention found that, differing from methods of the prior art, trace expressed protein and/or peptide, unable to be detected with methods of the prior art, can be detected and identified with high sensitivity by performing the claimed method.

B. Claimed Invention

The claimed invention recites the following (in part):

"A method for detecting, separating and identifying an expressed trace protein and/or peptide in a test sample, comprising:
converting a protein and/or peptide in a test sample to a fluorescent derivative,
separating said fluorescent derivative by a combination of HPLC and fluorescence detection (HPLC/fluorescence detection) to obtain fluorescent fractions,
applying the fluorescent fractions to mass spectrometry or MS/MS analysis, or applying the fluorescent fractions to enzymatic hydrolysis to obtain peptide fragments,
separating the peptide fragments to obtain peptide fractions, ..." (see claim 1).

As can be seen from claim 1 above, the fluorescent derivative (e.g., fluorescence labeled protein and/or peptide) is subjected to a separation step by a combination HPLC/fluorescence detection before a digestion step (e.g., enzymatic hydrolysis). The order of steps in the claimed process is specific and necessary due to the language/grammar of the claimed steps themselves as well as their description throughout the specification (see MPEP 2111.01, Part II). For example, the first "separating" step is performed "to obtain fluorescent fractions" and the following "applying" step is performed *on* said fluorescent fractions. Accordingly, by the nature of the language/grammar used in the claimed steps, the order of the processing steps is specific and necessary.

C. Differences Between the Claimed Invention and Patricelli Reference

In contrast to the claimed invention as described above, Patricelli discloses labeling proteins with a fluorescently labeled activity based probe (ABP), then digesting the ABP-labeled proteins, followed by separation (see col. 5, lines 23-24, "the labeled ABP-active target protein conjugates are most preferably proteolytically digested prior to the next stage of enrichment and/or analysis"; see also col. 15, lines 53-67). As such, Patricelli discloses digestion prior to separation and is silent with respect to separation prior to digestion.

Accordingly, as the order of steps in the claimed process is specific and necessary due to the language/grammar of the claimed steps themselves as well as their description in the specification (see above), and as Patricelli is silent with respect to Applicants' specifically claimed order, Patricelli can not then be considered to disclose or suggest such a different order. Therefore, Patricelli neither discloses nor suggests Applicants' processing limitations *as claimed.*

Thus, Applicants request withdrawal of the anticipation rejection over Patricelli and the obviousness rejection over Patricelli alone.

D. Remaining References Goodlett, Andersson and Toyo'oka

As explained above, Patricelli does not disclose or suggest the claimed processing order of separating the fluorescent derivative by HPLC/fluorescence detection *before* applying the fluorescent fractions obtained from the separation to enzymatic hydrolysis.

The Office relies upon Goodlett, Andersson and Toyo'oka merely for their alleged disclosures of the particulars of certain dependent claims, not for disclosure or suggestion of changing the processing order of the Patricelli reference. Applicants submit that these references are in fact silent with respect to Applicants' claimed processing order.

Accordingly, none of Goodlett, Andersson and/or Toyo'oka fulfill Patricelli's deficiency with respect to processing order. As such, no combination of these references discloses or suggests the claimed invention. Therefore, Applicants request withdrawal of the obviousness rejections relying upon such combinations of these references.

E. The Srinivasan Reference

Applicants note that Srinivasan was published on March 22, 2007, filed on September 16, 2005, and currently includes no claims of either domestic or foreign priority. The current

application has an effective U.S. filing date of December 13, 2004 (i.e., is the national stage of international PCT Application JP2004-018592). Accordingly, Srinivasan does not qualify as prior art against the current application. Thus, Applicants request withdrawal of any rejections relying upon this reference.

Conclusion

Applicants submit that all now-pending claims are in condition for allowance. Applicants respectfully request the withdrawal of the objections and rejections and passage of this case to issue.

Respectfully submitted,

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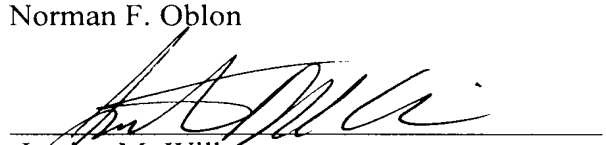

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